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Brief Communication

Aldehyde Dehydrogenase Polymorphism in North American, South American, and Mexican Indian Populations

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SUMMARY

While about 40% of the South American Indian populations (Atacameños, Mapuche, Shuara) were found to be deficient in aldehyde dehydrogenase isozyme I ($ALDH_2$ or E_2), preliminary investigations showed very low incidence of isozyme deficiency among North American natives (Sioux, Navajo) and Mexican Indians (mestizo). Possible implications of such trait differences on cross-cultural behavioral response to alcohol drinking are discussed.

INTRODUCTION

In our previous investigations, we reported on the absence of mitochondrial, low K_m, aldehyde dehydrogenase isozyme I ($ALDH_2$ or E_2) in about 50% of random Japanese autopsy liver specimens [1–4]. In subsequent population genetic studies using hair-root follicles, we found that this enzyme deficiency is widely prevalent among individuals belonging to the Mongoloid race only [5–10].

As the deficiency of ALDH I ($ALDH_2$ or E_2) isozyme has been implicated to

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be responsible for the high sensitivity to alcohol commonly observed among Japanese, Chinese, and Koreans [8–12], it seemed to us of interest to study ALDH polymorphism among American Indian populations generally regarded as subgroups of Mongoloids.

Here, we report the results of a pilot study on a few American Indian and Mexican Indian tribes regarding ALDH I ($ALDH_2$ or E_2) isozyme deficiency in comparison with data from other populations.

MATERIALS AND METHODS

Samples of hair roots (30–40 hairs each) were collected from different population groups and were analyzed immediately or transported in dry ice to Hamburg by air. Analyses were completed within 1 week of sample collection. The hair samples of Sioux and Navajo Indians were collected from North Dakota and New Mexico, respectively. The hair samples of mestizo were collected in Mexico City. The hair samples of Atacameños were collected in Toconao in the Atacama desert, Chile, from Mapucho in the area of Valdivia, Chile, and of Shuara from Ecuador.

Separation and detection of ALDH isozymes in hair-root lysates was carried out as described [8, 13]. Malate dehydrogenase (MDH) activity was determined in all the hair-root lysates to give a reliable estimate of the presence or the absence of mitochondrial enzymes [5, 14].

RESULTS

The frequency of ALDH I ($ALDH_2$ or E_2) in different native American populations is shown in table 1. For the sake of comparison, published and unpublished data on the incidence of ALDH I isozyme deficiency in various Mongoloid, Caucasoid, and Negroid populations are also included.

As evident from the table, individuals belonging to Caucasoid and Negroid races show no isozyme deficiency but the enzyme was found widely missing in hair roots of Mongoloid subjects.

Among native Indians, about 40% of the South American Indian tribes (Mapuche, Atacameños, Shuara) showed ALDH deficiency. However, a very small percentage of isozyme deficiency was detected in Sioux, Navajo, and mestizo tribes.

DISCUSSION

It is commonly accepted that American Indians represent a subgroup of the Mongoloid race [17]. They migrated from northeast Asia 30,000–40,000 years ago, and some of them came 8,000–15,000 years ago [18]. Because of genetic drift, they diverged rapidly, and the present Amerind populations are considerably different from the Asian Mongoloid populations. In other words, they have undergone extensive differentiation [19].

The present-day North American Indian populations represent an admixture of native Indians and Caucasoids of European origin, and the modern South American Indian populations represent a hybrid of Caucasoids, Negroids, and Mongoloids. Genetic distances between North American Indians and South American Indians is very large compared with distances seen between Asiatic Mongoloid populations [20].

Alcohol abuse and alcoholism are major problems among American Indian

TABLE 1

FREQUENCY OF ALDH ISOZYME DEFICIENCY IN AMERICAN INDIANS, ASIAN MONGOLOIDS, AND OTHER POPULATIONS

Population	Sample size	Percent deficient	Reference
South American Indians:			
Atacameños (Chile)	133	43	[6]
Mapuche (Chile)	64	41	[7]
Shuara (Ecuador)	99	42	[8]
North American Indians:			
Sioux (North Dakota)	90	5	Present study
Navajo (New Mexico)	56	2	Present study
Mexican Indians:			
Mestizo (Mexico City)	43	4	Present study
Asian Mongoloids:			
Japanese	184	44	[1, 3, 9]
Chinese:			
Mongolian	198	30	[10]
Zhuang	106	45	[10]
Han	120	50	[10]
Korean (Mandschu)	209	25	[10]
Chinese, living abroad	196	35	[8]
Koreans (South Korea)	75	27	[15]
Vietnamese	138	53	[8]
Indonesians	30	39	[8]
Thais (North)	110	8	[8]
Filippinos	110	13	Present study
Ainu	80	20	Present study
Other populations:			
Germans	300	0	[8]
Egyptians	260	0	[8]
Sudanese	40	0	[8]
Kenyans	23	0	[8]
Liberians	184	0	[8]
Turks	65	0	Present study
Fangs	37	0	Present study
Israeli	77	0	Present study
Hungarians	177	0	[16]
Matyo	106	0	[16]
Romai	84	0	[16]
Asian Indians	50	0	Present study

tribes [21, 22]. American and Mexican Indians have been found to metabolize alcohol faster than Caucasian groups [23–25]. Like the majority of Mongoloids (Japanese, Chinese, Koreans), American Indians are also sensitive to alcohol and exhibit facial flushing associated with various subjective and objective vasomotor symptoms after drinking moderate amounts of alcohol [26, 27].

Since the deficiency of ALDH I ($ALDH_2$ or E_2) isozyme has been so far found to be exclusively confined to subjects of Mongoloid race, it is of significant interest to note that Sioux and Navajo tribes and the mestizo group show a very low percentage of isozyme deficiency while native Americans from Chile and Ecuador were found deficient to an extent comparable with Japanese and Chinese.

In recent preliminary reports, other authors have found either no deficiency of ALDH I isozyme in autopsy livers of American Indians of northern New Mexico [28] or only up to 16% deficiency in hair roots of Oklahoma Indians [29].

Although considerable differences in the drinking habits of native American Indians as compared to the so-called whites have been observed over centuries, no significant difference between North and South American Indians regarding drinking pattern and behavioral outcome can be pointed out [21].

A significantly lower incidence of ALDH I isozyme deficiency was observed in a group of Japanese alcoholics than in psychiatric patients, drug dependents, and healthy controls [9, 30]. Individuals sensitive to alcohol by virtue of their genetically controlled deficiency of a key enzyme of alcohol metabolism may be discouraged from abuse of alcohol due to initial aversive reactions.

Whether ALDH isozyme deficiency also plays a similar protective role among native Americans has yet to be understood. Moreover, it remains to be explained why the South American Indian tribes show widespread ALDH isozyme deficiency similar to Mongoloids while their North American counterparts show significantly low incidence of such isozyme abnormality.

To better understand the evolutionary role of aldehyde dehydrogenase deficiency in alcohol dependence—protective or reinforcing—more native American Indian populations have to be investigated concerning ALDH I ($ALDH_2$ or E_2) deficiency, alcohol sensitivity, drinking habits, and the rate of alcoholism.

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REFERENCES

1. Goedde HW, Harada S, Agarwal DP: Racial differences in alcohol sensitivity: a new hypothesis. *Hum Genet* 51:331–334, 1979
2. Harada S, Misawa S, Agarwal DP, Goedde HW: Liver alcohol dehydrogenase and aldehyde dehydrogenase in Japanese: isozyme variation and its possible role in alcohol intoxication. *Am J Hum Genet* 32:8–15, 1980
3. Agarwal DP, Harada S, Goedde HW: Racial differences in biological sensitivity to ethanol: the role of alcohol dehydrogenase and aldehyde dehydrogenase isozymes. *Alcoholism: Clin Exp Res* 5:12–16, 1981
4. Agarwal DP, Eckey R, Harada S, Goedde HW: Basis of aldehyde dehydrogenase deficiency in Orientals: immunochemical studies. *Alcohol* 1:111–118, 1984
5. Goedde HW, Agarwal DP, Eckey R, Harada S: Population genetic and family studies on aldehyde dehydrogenase deficiency and alcohol sensitivity. *Alcohol* 2:383–390, 1985
6. Goedde HW, Rothhammer F, Benkmann HG, Bogdanski P: Ecogenetic studies in Atacameno Indians. *Hum Genet* 67:343–346, 1984
7. Goedde HW, Montaya Ogalde V, Benkmann HG: Population genetic studies in Mapuche Indians. Submitted for publication
8. Goedde HW, Agarwal DP, Harada S, et al.: Population genetic studies on al-

dehyde dehydrogenase isozyme deficiency and alcohol sensitivity. *Am J Hum Genet* 35:769–772, 1983
9. GOEDDE HW, AGARWAL DP, HARADA S: The role of alcohol dehydrogenase and aldehyde dehydrogenase isozymes in alcohol metabolism, alcohol sensitivity and alcoholism, in *Isozymes: Current Topics in Biological Medicine Research,* vol 8, *Cellular Localization, Metabolism, and Physiology,* New York, Alan R. Liss, 1983, pp 175–193
10. GOEDDE HW, BENKMANN HG, KRIESE L, ET AL.: Aldehyde dehydrogenase isozyme deficiency and alcohol sensitivity in four different Chinese populations. *Hum Hered* 34:183–186, 1984
11. HARADA S, AGARWAL DP, GOEDDE HW: Aldehyde dehydrogenase deficiency as cause of facial flushing reaction to alcohol in Japanese. *Lancet* ii:982, 1981
12. MIZOI Y, TATSUNO Y, ADACHI I, ET AL.: Alcohol sensitivity related to polymorphism of alcohol-metabolizing enzymes in Japanese. *Pharmacol Biochem Behav* 18, Suppl 1:127–133, 1983
13. GOEDDE HW, AGARWAL DP, HARADA S: Genetic studies on alcohol metabolizing enzymes: detection of isozymes in human hair roots. *Enzyme* 25:281–286, 1980
14. YOSHIDA A: Determination of aldehyde dehydrogenase phenotypes using hair roots: re-examination. *Hum Genet* 66:296–299, 1984
15. GOEDDE HW, AGARWAL DP, PAIK YK: Frequency of aldehyde dehydrogenase I isozyme deficiency in Koreans. A pilot study. *Korean J Genet* 5:88–90, 1983
16. CZEIZEL A, BENKMANN HG, GOEDDE HW, ET AL.: Ecogenetic and population genetic studies in Hungary. Submitted for publication
17. ZEGURA S: in *Out of Asia. Peopling Americas and the Pacific,* edited by KIRK R, SZATHMARY E, Canberra, Australia, Journal of Pacific History, 1985, pp 1–19
18. WILLIAMS RC, STEINBERG AG, GERSHOWITZ H, ET AL.: GM allotypes in native Americans: evidence for three distinct migrations across the Bering land bridge. *Am J Phys Anthropol* 66:1–19, 1985
19. JOHNSON MJ, WALLACE DC, FERRIS SD, RATTAZZI MC, CAVALLI-SFORZA LL: Radiation of human mitochondria DNA types analyzed by restriction endonuclease cleavage patterns. *J Mol Evol* 19:255–271, 1983
20. NEI M, ROYCHOUDHURY AK: Genetic relationship and evolution of human races, in *Evolutionary Biology,* edited by HECHT MK, WALLACE B, PRANCE GT, New York, Plenum Press, 1982, pp 1–59
21. EVERETT MW, WADDEL JO, HEATH DB: *Cross-cultural Approaches to the Study of Alcohol.*The Hague, Paris, Mouton, 1976
22. WHITTAKER JO: Alcohol use and the American Indian—some socio-cultural lessons about the nature of alcoholism. *Br J Alcohol and Alcoholism* 14:140–147, 1979
23. FARRIS JJ, JONES BM: Ethanol metabolism in male American Indians and whites. *Alcoholism: Clin Exp Res* 2:77–82, 1978
24. HANNA JM: Metabolic responses of Chinese, Japanese and Europeans to alcohol. *Alcoholism: Clin Exp Res* 2:89–92, 1978
25. REED TE: Racial comparisons of alcohol metabolism: background, problems and results. *Alcoholism: Clin Exp Res* 2:61–69, 1978
26. WOLFF P: Ethnic differences in alcohol sensitivity. *Science* 175:449–450, 1972
27. WOLFF P: Vasomotor sensitivity to alcohol in diverse Mongoloid populations *Am J Hum Genet* 25:193–199, 1973
28. REX DK, SMIALEK JE, BOSRON WF, LI TK: Alcohol and aldehyde dehydrogenase isozymes in a North American Indian population. Second Congress of the International Society for Biomedical Research on Alcoholism, Santa Fe, New Mexico, 1984, abstr. no. 216, p 115
29. ZEINER AR, GIRARDOT JM, NIEHOLS N, JONES-SAUMTY D: ALDH I isozyme deficiency among North American Indians. Ibid., abstr. no. 300, p 129
30. HARADA S, AGARWAL DP, GOEDDE HW, TAGAKI S, ISHIKAWA B: Possible protective role against alcoholism for aldehyde dehydrogenase isozyme deficiency in Japan. *Lancet* ii:827, 1982